REMARKS

Claims 1, 2, and 21 have been amended. Support for the amendments can be found in the Specification as filed: in Example 1, page 17-18, and in Example 4, page 23 lines 24-27. Therefore, no new matter has been introduced herewith. As a result, Claims 1-4 and 21-22 are presented for the examination. The following addresses the substance of the Office Action.

Claim Rejections under 35 U.S.C. §112

The Examiner has rejected Claims 1-4, 21 and 22 under 35 U.S.C. §112, first paragraph. More specifically, the Examiner argued that though the Specification is enabling for the *in vitro* inhibition of p38 MAP kinase following administration of pyridinylimidazole compounds, whereby Nontypeable *Haemophilus influenzae* (NTHi) cytoplasmic protein induction of mucin MUC5AC transcription is inhibited, it does not provide enablement for the treatment of mucin overproduction in any mammal comprising administration of a pyridinylimidazole inhibitor of p38 MAP kinase to any mammal. The Examiner also stated that "the art (...) is silent with respect to the *in vivo* administration, targeting and subsequent inhibition of p38 MAP kinase by pyridinylimidazole compounds, as well as with respect to the *in vivo* treatment of overproduction of mucin using pyridinylimidazole inhibitors of p38 MAP kinase". The Examiner further argued that it would require undue trial and error and undue experimentation to practice the invention drawn to any route of administration of the claimed pyridinylimidazole inhibitors of p38 MAP kinase in a mammal, so that mucin overproduction is inhibited. Specifically, the Examiner contended that determination of accessible target sites, modes of *in vivo* delivery and formulations of p38 MAP kinase inhibitors effective in inhibiting expression of mucins in a mammal would require undue experimentation in the unpredictable field of *in vivo* delivery and treatment effects of p38 MAP kinase inhibitors. The Applicants respectfully disagree.

Objective evidence in support of enablement of the Claims

Applicants submit that the Declaration of Jian-Dong Li, dated May 5, 2004 filed herewith, provides proof that Claims 1-4 and 21-22 as currently amended are enabled. In particular, as provided in the Declaration, the intraperitoneal (systemic) administration of a specific p38 inhibitor, SB203580, to mice before inoculation of their lungs with NTHi, an experimental model of chronic obstructive pulmonary disease (COPD), greatly inhibited NTHi-induced *MUC5AC* expression in the lung of the mice. In addition, the inventor stated that the pharmacological effects of pyridinylimidazole inhibitors of p38 MAP kinase *in vivo* are well-

studied and described in the art (see the abstracts of exemplary articles attached). In fact, they are currently tested in several clinical trials in humans for various diseases. Therefore, the specific dosages, modes of *in vivo* delivery and formulations of p38 MAP kinase inhibitors, though labor-intensive and tedious, can be determined in these and similar trials and do not require undue experimentation because they are well within the level of a skilled artisan capable of following the instructions of Remington's Pharmaceutical Sciences, Meade Publishing Co., Easton, Pa.

Therefore, Claims 1-4 and 21-22 as currently amended are fully enabled for the scope claimed, and the rejection under 35 U.S.C. §112, first paragraph should be withdrawn.

CONCLUSION

In view of the foregoing, Applicant respectfully requests that this application be passed to issuance. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 6, 2004

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